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PATENT

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Joseph E. Zahner
Reg. No. 48,224
7733 Forsyth Boulevard
Suite 1400
St. Louis, Missouri 63105
(314) 727-5188

In re application of:
Milbrandt and Baloh

Serial No.: 09/473,551

Filed: December 28, 1999

For: GFR(alpha)1-RET SPECIFIC AGONISTS AND METHODS THEREFOR

Examiner Olga N. Chernyshev

Group Art Unit 1646

BOX PETITION TO COMMISSIONER
Assistant Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

PETITION FROM REQUIREMENT FOR RESTRICTION UNDER 37 C.F.R. 1.144

Petitioner hereby respectfully requests the Commissioner to review the requirement for restriction to a single molecular embodiment of a growth factor in the instant application. A declaration from Dr. Jeff Milbrandt (Exhibit A) and a sequence alignment of the specific growth factor molecular embodiments under dispute (Exhibit B) are herewith submitted.

Facts of the case

In the office action of paper no. 10, the Examiner required applicant to elect a single group of claims (I-XX). Applicants elected group I, which claims are drawn to a growth factor that activates GFRα1-RET. However, in addition to the election of a group of claims, the Examiner, in bullet point number 13 of the detailed action of paper number 10, further required a restriction to "a single molecular embodiment" of the growth factor that activates GFRα1-RET. The bullet point number 13 is reproduced below:

> "The claims of groups I-XX are drawn to a multitude of growth factors (SEQ ID NO:1-28), polynucleotides encoding such, and methods of using the growth factor/polynucleotide encoding/cell containing the polynucleotide encoding. This constitutes recitation of an implied, mis-joined Markush group that contains multiple, independent and distinct inventions. Each of the different growth factors/nucleic acids/ and methods of use are independent and distinct because no common structural or functional properties are shared. Burden is established because each growth factor has a unique sequence, and therefore, requires a separate search, as is the same for the encoding polynucleotide and methods of use. Accordingly, these claims are subject to restriction under 35 U.S.C. § 121.
>
> "Upon election of one of groups I-XX, Applicant is additionally required to elect a single growth factor or polynucleotide (i.e. single molecular embodiment which may be represented by a sequence identifier). This requirement is not to be construed as a requirement for an election of species, since each of the compounds recited in alternative form is not a member of a single genus of invention." (Examiner's detailed action of paper number 10).

In the response to this restriction requirement, Applicants traversed the "single molecular embodiment" restriction. Applicants consider that this restriction is most appropriately a species election, not an election restriction. This position taken by the Applicants is based upon their experience prosecuting similar growth factor cases before the USPTO in which multiple species homologues of novel growth factors were *always* treated as a single invention. The traversal of the restriction requirement for a "single molecular embodiment" of the claimed growth factor, which was filed on July 30, 2001 in response to paper number 10 , is reproduced below:

"Applicants argue that all of the growth factor embodiments of the elected claims are *not* independent inventions, as promulgated by the Patent Office on page eight (8), first paragraph, but rather species comprising a single genus as defined in the "linking" claims 1 and 2. Wherein claim1 is drawn to a growth factor, which activates only GFRα1-RET and claim 2 is further drawn to a chimeric growth factor comprised of GDNF family members or derivatives thereof, the multiple embodiments presented in the subsequent claims are merely species of the genus presented in each of claims 1 and 2. Furthermore and quite simply, the invention is drawn to a persephin with its F2a and F2c regions substituted for the F2a and F2c regions of GDNF family members which engage the GFRα1-RET receptor. This enables the substituted persephin to engage only GFRα1-RET, a completely novel activity disclosed in the instant application.

"Applicants submit that human, mouse and rat persephin (SEQ ID NO:1-3) are a reasonable number of species within the genus of persephin. Likewise, applicants submit that GDNF, neurturin and artemin are a reasonable number of species comprising the GDNF family of growth factors. However, the invention is not claiming persephin, GDNF, neurturin and artemin, and all chimerical combinations thereof, but merely claims a persephin that contains specific combinations of eleven to twelve amino acid substitutions that span a very narrow portion of the molecule namely the F2a and F2c regions, wherein each set of substitutions confers GFRα1 specificity.

"Given the genus claims 1 and 2, and the reasonableness of the number of species within the genus, namely three substituted persephins, wherein each persephin may comprise 1 of 3 possible substitutions, Applicants respectfully submit that the election requirement related to the elected invention number I is not warranted. Applicants therefore respectfully request that this restriction requirement, as stipulated on page eight (8), paragraph one (1), be reconsidered and withdrawn." (Response to office action of paper number 10, filed July 30, 2001).

In the office action of paper number 13, the Examiner disagreed with Applicants' argument "because in the instant case the different forms of persephin (human, mouse and rat) are representing chemically, structurally and functionally different compounds, which can be made and used without each other, therefore representing patentably distinct inventions itself. It is therefore concluded that claimed different persephin molecular embodiments containing specific amino acid substitutions constitute independent and patentably distinct inventions, since they all have different chemical

structures, different functions, and can be made and used without each other (see MPEP § 808.01)," from Detailed Action of paper no. 13, page 2, bullet point number 1).

New arguments and evidence

Petitioners respectfully request that the Commissioner review this restriction requirement. According to the declaration of Dr. Jeff Milbrandt (Exhibit A), an inventor of the instant invention and a neurotrophic growth factor specialist of 20 years, the human, rat and mouse persephins are considered to be species of the very same growth factor called persephin. In the art, growth factors with close amino acid identity or similarity that are produced in closely related species of animals, such as mammals (including humans, rats and mice), are considered to be functional homologues that have the same biological activity and tertiary chemical structure. According to Dr. Milbrandt, those growth factors that show at least greater than 80% identity at the amino acid level are homologues of the same growth factor. Furthermore, in the neurotrophic growth factor patent applications submitted by Dr. Milbrandt (including applications directed to persephin itself), which have genus claims to growth factors as well as claims to specific sequences directed to species of mammalian homologues, no requirement to elect an invention based upon a specific molecular entities as defined by sequence identifiers or no requirement to elect a species was ever issued in any of these cases.

Upon comparing the sequences of human, rat and mouse persephin (see Exhibit B), those sequences are at least 94% similar to each other, and therefore are considered by one of ordinary skill in the art of growth factor biology to be essentially the same growth factor. Petitioners argue that the human, mouse and rat sequences presented in the instant application are obvious embodiments of the same growth factor and are thus not patentably distinct. Furthermore, Applicants believe that restricting the claims to a single sequence embodiment places an unfair burden upon the small entity inventor to submit applications for each and every species embodiment of the claimed growth factor, which is not in the spirit of the American Inventors Protection Act of 1999.

Conclusion

Petitioners believe that the restriction requirement imposed by the Examiner in this case, specifically regarding the specific molecular entities of functional and structural homologues, is not appropriate. Petitioners respectfully request that the Commissioner review and reverse this requirement.

The Commissioner is invited to call the undersigned agent to discuss any issues related to this matter.

Respectfully submitted,

Joseph E. Zahner
Reg. No. 48,224
Thompson Coburn LLP
7733 Forsyth Boulevard, Suite 1400
St. Louis, Missouri 63105
(314) 727-5188

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